

CLAIMS

What is claimed is:

1. A method of characterizing a nucleic acid sequence that encodes a Na_v1.7 sodium channel alpha subunit, comprising the step of identifying mutations at one or more sites in regions of the nucleic acid sequence that encode an intracellular *N*-terminal region, an extracellular loop in domain I, an intracellular loop between domains I and II, an intracellular loop between domains II and III, an intramembrane region of domain II, or any combination thereof, such identified nucleotides indicating the character of the nucleic acid sequence.
2. The method of claim 1, wherein the mutation is present in the nucleic acid region encoding the intracellular *N*-terminus region of the subunit.
3. The method of claim 2, wherein the mutation encodes amino acid residue 62.
4. The method of claim 3, wherein the encoded amino acid residue is valine.
5. The method of claim 1, wherein the mutation is present in the nucleic acid region encoding the extracellular loop of domain I of the subunit.
6. The method of claim 5, wherein the mutation encodes amino acid residue 149.
7. The method of claim 6, wherein the encoded amino acid residue is glutamine.
8. The method of claim 1, wherein the mutation is present in the nucleic acid region encoding the intracellular loop between domains I and II of the subunit.
9. The method of claim 8, wherein the mutation encodes amino acid residue 641.
10. The method of claim 9, wherein the encoded amino acid residue is tyrosine.
11. The method of claim 8, wherein the mutation encodes amino acid residue 655.
12. The method of claim 11, wherein the encoded amino acid residue is arginine.
13. The method of claim 1, wherein the mutation is present in the nucleic acid region encoding the intracellular loop between domains II and III of the subunit.
14. The method of claim 13, wherein the mutation encodes amino acid residue 1123.
15. The method of claim 14, wherein the encoded amino acid residue is phenylalanine.
16. The method of claim 1, wherein the mutation is present in the nucleic acid region encoding the intramembrane region of domain II of the subunit.
17. The method of claim 16, wherein the mutation encodes amino acid residue 739.
18. The method of claim 17, wherein the encoded amino acid residue is valine.
19. The method of claim 1, wherein the step of identifying the mutations comprises comparing the nucleic acid sequence to a wild-type nucleic acid sequence.

20. The method of claim 19, wherein the wild-type nucleic acid sequence encodes the amino acid sequence of SEQ ID NO: 38.
21. The method of claim 1, wherein the identifying step comprises obtaining a biological sample and testing the sample to identify the nucleotides at the mutations sites of the nucleic acid contained therein.
22. The method of claim 21, wherein the sample is tested by sequencing or probing the nucleic acid.
23. The method of claim 22, wherein the testing step comprises the step of amplifying the nucleic acid contained in the sample.
24. The method of claim 23, wherein the testing step further comprises sequencing the amplified nucleic acid.
25. The method of claim 23, wherein the amplifying step comprises a polymerase chain reaction (PCR).
26. The method of claim 23, wherein the amplifying step comprises contacting the nucleic acid with a primer comprising one or more of the sequences of SEQ ID NOs: 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, and 31.
27. A method for determining a Na_v1.7 haplotype in a human subject comprising identifying one or more nucleotides encoding amino acid residues 62, 149, 641, 655, 739, 1123, or any combination thereof, wherein the nucleotide or nucleotides indicate the haplotype.
28. A method for determining a subject's predisposition to a neurologic disorder associated with a sodium channel mutation comprising comparing the subject's Na_v1.7 haplotype with one or more reference haplotypes that correlate with the neurologic disorder, a similar haplotype in the subject's Na_v1.7 haplotype as compared to the reference haplotype or haplotypes indicating a predisposition to the neurologic disorder.
29. The method of claim 28, wherein the neurologic disorder is a seizure disorder.
30. The method of claim 29, wherein the seizure disorder is a febrile seizure disorder.
31. The method of claim 28, wherein the reference haplotype comprises nucleotides that encode one or more mutations at residue 62, residue 149, residue 641, residue 655, residue 739, or residue 1123 of the encoded amino acid sequence of Na_v1.7.
32. A method of identifying a compound that modulates mutant Na_v1.7 sodium channels comprising:
 - a) contacting with a test compound a cell containing a mutant Na_v1.7 nucleic

- acid that encodes a mutant Na_v1.7 sodium channel comprising one or more mutations at residue 62, residue 149, residue 641, residue 655, residue 739, or residue 1123;
- b) detecting Na_v1.7 sodium channel activity; and
- c) comparing the Na_v1.7 sodium channel activity in the contacted cell with the amount of Na_v1.7 sodium channel activity in a control cell, wherein the control cell is not contacted by the test compound, an increased or decreased Na_v1.7 sodium channel activity in the test cell as compared to the control cell indicating a compound that modulates mutant Na_v1.7 sodium channels.
33. An isolated nucleic acid comprising a nucleotide sequence encoding the amino acid sequence of SEQ ID NO: 2.
34. An isolated nucleic acid comprising a sequence that hybridizes under stringent conditions to the nucleic acid of claim 33 but not to the nucleic acid sequence that encodes SEQ ID NO: 38.
35. An expression vector comprising the nucleic acid of claim 33 operably linked to an expression control sequence.
36. A cultured cell comprising the vector of claim 35.
37. A method of making a mutant Na_v1.7 sodium channel alpha subunit comprising culturing the cell of claim 36 under conditions allowing expression of the polypeptide encoded by the nucleic acid, wherein the polypeptide comprises a mutant Na_v1.7 sodium channel.
38. An isolated nucleic acid comprising a nucleotide sequence encoding at least 5 residues of the amino acid sequence of SEQ ID NO: 2, wherein one of the amino acid residues comprises a valine in a position that corresponds to position 62 in SEQ ID NO: 2.
39. An isolated nucleic acid comprising a nucleotide sequence encoding the amino acid sequence of SEQ ID NO: 3.
40. An isolated nucleic acid comprising a sequence that hybridizes under stringent conditions to the nucleic acid of claim 39 but not to the nucleic acid sequence that encodes SEQ ID NO: 38.
41. An expression vector comprising the nucleic acid of claim 39 operably linked to an expression control sequence.
42. A cultured cell comprising the vector of claim 41.

43. A method of making a mutant Na_v1.7 sodium channel alpha subunit comprising culturing the cell of claim 42 under conditions allowing expression of the polypeptide encoded by the nucleic acid, wherein the polypeptide comprises a mutant Na_v1.7 sodium channel.
44. An isolated nucleic acid comprising a nucleotide sequence encoding at least 5 residues of the amino acid sequence of SEQ ID NO: 3, wherein one of the amino acid residues comprises a glutamine in a position that corresponds to position 149 in SEQ ID NO: 3.
45. An isolated nucleic acid comprising a nucleotide sequence encoding the amino acid sequence of SEQ ID NO: 4.
46. An isolated nucleic acid comprising a sequence that hybridizes under stringent conditions to the nucleic acid of claim 45 but not to the nucleic acid sequence that encodes SEQ ID NO: 38.
47. An expression vector comprising the nucleic acid of claim 45 operably linked to an expression control sequence.
48. A cultured cell comprising the vector of claim 47.
49. A method of making a mutant Na_v1.7 sodium channel alpha subunit comprising culturing the cell of claim 48 under conditions allowing expression of the polypeptide encoded by the nucleic acid, wherein the polypeptide comprises a mutant Na_v1.7 sodium channel.
50. An isolated nucleic acid comprising a nucleotide sequence encoding at least 5 residues of the amino acid sequence of SEQ ID NO: 4, wherein one of the amino acid residues comprises a tyrosine in a position that corresponds to position 641 in SEQ ID NO: 4.
51. An isolated nucleic acid comprising a nucleotide sequence encoding the amino acid sequence of SEQ ID NO: 5.
52. An isolated nucleic acid comprising a sequence that hybridizes under stringent conditions to the nucleic acid of claim 51 but not to the nucleic acid sequence that encodes SEQ ID NO: 38.
53. An expression vector comprising the nucleic acid of claim 51 operably linked to an expression control sequence.
54. A cultured cell comprising the vector of claim 53.
55. A method of making a mutant Na_v1.7 sodium channel alpha subunit comprising culturing the cell of claim 54 under conditions allowing expression of the

- polypeptide encoded by the nucleic acid, wherein the polypeptide comprises a mutant Na_v1.7 sodium channel.
56. An isolated nucleic acid comprising a nucleotide sequence encoding at least 5 residues of the amino acid sequence of SEQ ID NO: 5, wherein one of the amino acid residues comprises a arginine in a position that corresponds to position 655 in SEQ ID NO: 5.
57. An isolated nucleic acid comprising a nucleotide sequence encoding the amino acid sequence of SEQ ID NO: 6.
58. An isolated nucleic acid comprising a sequence that hybridizes under stringent conditions to the nucleic acid of claim 57 but not to the nucleic acid sequence that encodes SEQ ID NO: 38.
59. An expression vector comprising the nucleic acid of claim 57 operably linked to an expression control sequence.
60. A cultured cell comprising the vector of claim 59.
61. A method of making a mutant Na_v1.7 sodium channel alpha subunit comprising culturing the cell of claim 60 under conditions allowing expression of the polypeptide encoded by the nucleic acid, wherein the polypeptide comprises a mutant Na_v1.7 sodium channel.
62. An isolated nucleic acid comprising a nucleotide sequence encoding at least 5 residues of the amino acid sequence of SEQ ID NO: 6, wherein one of the amino acid residues comprises a valine in a position that corresponds to position 739 in SEQ ID NO: 6.
63. An isolated nucleic acid comprising a nucleotide sequence encoding the amino acid sequence of SEQ ID NO: 7.
64. An isolated nucleic acid comprising a sequence that hybridizes under stringent conditions to the nucleic acid of claim 63 but not to the nucleic acid sequence that encodes SEQ ID NO: 38.
65. An expression vector comprising the nucleic acid of claim 63 operably linked to an expression control sequence.
66. A cultured cell comprising the vector of claim 65.
67. A method of making a mutant Na_v1.7 sodium channel alpha subunit comprising culturing the cell of claim 67 under conditions allowing expression of the polypeptide encoded by the nucleic acid, wherein the polypeptide comprises a mutant Na_v1.7 sodium channel.

68. An isolated nucleic acid comprising a nucleotide sequence encoding at least 5 residues of the amino acid sequence of SEQ ID NO: 7, wherein one of the amino acid residues comprises a phenylalanine in a position that corresponds to position 1123 in SEQ ID NO: 7.
69. A transgenic mouse comprising cells that encode a mutant Na_v1.7 sodium channel alpha subunit, wherein the mouse exhibits increased seizure activity as compared to the wild-type mouse.
70. An isolated polypeptide comprising SEQ ID NO: 2.
71. An isolated polypeptide comprising SEQ ID NO: 32.
72. An isolated polypeptide comprising SEQ ID NO: 3.
73. An isolated polypeptide comprising SEQ ID NO: 33.
74. An isolated polypeptide comprising SEQ ID NO: 4.
75. An isolated polypeptide comprising SEQ ID NO: 34.
76. An isolated polypeptide comprising SEQ ID NO: 5.
77. An isolated polypeptide comprising SEQ ID NO: 35.
78. An isolated polypeptide comprising SEQ ID NO: 6.
79. An isolated polypeptide comprising SEQ ID NO: 36.
80. An isolated polypeptide comprising SEQ ID NO: 7.
81. An isolated polypeptide comprising SEQ ID NO: 37.
82. A purified antibody that selectively binds to an epitope of a mutant Na_v1.7 sodium channel alpha subunit.
83. The antibody of claim 82, wherein the mutant is an I62V mutant.
84. The antibody of claim 82, wherein the mutant is an P149Q mutant.
85. The antibody of claim 82, wherein the mutant is an N641Y mutant.
86. The antibody of claim 82, wherein the mutant is an K655R mutant.
87. The antibody of claim 82, wherein the mutant is an I739V mutant.
88. The antibody of claim 82, wherein the mutant is an L1123F mutant.